REMARKS

Claim 30 has been amended to correct the tense of the word "oligonucleotide". This amendment corrects a typographical error and does not involve new matter.

112 Rejection, 1st Paragraph – Written Description

Claims 24 and 28-32 have been rejected under 35 USC 112, first paragraph as containing subject matter not described in the Specification. The Office Action indicates that Claim "34" has been rejected but the Applicants believe that that is a typographical error as there is no Claim 34 in the present application and the prior Office Action rejected Claim 24. The Applicants will treat the rejection as one to Claim 24. In particular, the Examiner alleges that the Claims should be limited to only the mixed duplex oligonucleotides (hereinafter MDON) specified in the Specification. The Examiner has also cited MPEP Section 2163 in support of the rejection. This rejection is respectfully traversed.

The Applicants prior arguments are still deemed relevant and are incorporated herein by reference. The Examiner's citation to MPEP Section 2163 is not warranted. First, the present claims do not describe the invention solely in terms of a method of its making coupled with it's function. Second, the USPTO has issued at least two US Patents in the gene repair (chimeraplasty) art that have similar language regarding inventions to altering genes *in situ*. US Patent 3,565,350, Claim 12, is set forth below:

> "12. A method of introducing a predetermined alteration in a target sequence of the genome of a cultured cell, which cell contains a nucleus, which comprises the steps of: a) providing mixed ribo-deoxyribonucleic acid vector having two regions homologous with a target sequence and a heterologous region, disposed there

> between, encoding the alternation; and b) maintaining the mixed ribo-deoxyribonucleic acid vector within the nucleus of the cultured cell, whereby the alteration is introduced into the target sequence."

It is readily apparent that one of ordinary skill in the art would recognize a correlation between the "mixed ribo-deoxyribonucleic acid vector," that contains both homologous and heterologous regions to the native gene desired to be changed, and the corresponding change in the native gene. The skilled artisan would certainly understand that any gene could be changed by the vector described in the '350 patent as taught and claimed in Claim 12 thereof. If Claim 12 of the '350 patent meets the requirements of Section 112 then certainly the present claims do as well. The claims of the '350 patent are not limited to the specific vectors or specific genes disclosed in the '350 patent Specification. The priority date of the '350 patent is 9 December 1994.

Additionally, US Patent 5,731,181 contains Claim 24 set forth below:

> "30. A method of introducing an alteration in a target sequence of the genome of a plant cell, which comprises the steps of: a) providing the oligonucleobase of claim 9, which further comprises two regions homologous with a target sequence and a mutator region, disposed there between, encoding the alteration; and b) maintaining said oligonucleobase within the nucleus of the cell, whereby the alteration is introduced in the target sequence."

The same reasoning described above to the '350 patent apply to the '181 patent where the additional teaching of altering plant genes is disclosed and claimed in the '181 patent. The priority of the '181 patent is 17 June 1996.

It is very clear that the invention as claimed is adequately described in the present Specification and that one of ordinary skill in the art would expect the claimed subject matter to be supported by the Specification. Withdrawal of this rejection is respectfully requested.

112 Rejection – Enablement

Claims 24 and 28-32 have been rejected under 35 USC 112, first paragraph for being non-enabling. The Examiner has cited In re Fisher for the proposition that the claims must bear a reasonable correlation to the scope of enablement provided by the Specification. This rejection is respectfully traversed.

The Applicants prior arguments are still deemed relevant and are incorporated herein by reference. The Examiner has cited the Fisher decision and has pointed out that the Applicants have failed to teach a high degree of predictability in the art to which the present claims are directed. As indicated above, the '350 and the '181 patents teach the use of gene repair in general and the use of gene repair in plants, respectively. The "vectors" and MDON are similar. Both of these prior issued US Patents are described in the Specification from pages 1-3. It appears to the Applicants that the present 112 rejection may have been relevant to the claims in the Kmiec patents ('350 and '181 patents) but not in the present application. Just like in the '350 and '181 patents, the scope of the present claims with respect to the MDON and the gene altered is broad and is not limited to a specific gene or a specific MDON. If the '351 and '181 patents meet the requirements of 112 then the present claims do also. Of course, the present claims are also non-obvious over the '350 and '181 patents as argued in prior correspondence with the Office and as argued below. Withdrawal of this rejection is respectfully requested.

102 Rejection – Hawkes et al

Claims 30-32 have been rejected under 35 USC 102(a) as being anticipated by Hawkes et al (WO 98/54330). The Examiner incorrectly states that Hawkes et al

inherently discloses plant microspores being treated with MDON. This rejection is respectfully traversed.

Hawkes et al describe treating maize **pollen** with MDON. No where does Hawkes et al teach or disclose treating microspores with MDON. Microspores are distinct from pollen. A pollen grain is a highly differentiated structure. Pollen develop from a nuclear mitotic division occurring in microspores. This division clearly produces a bi-nucleate structure consisting of a generative cell and a tube cell nucleus. Upon germination of the pollen grain, which occurs when it contacts a receptive female reproductive structure, a cell membrane then forms around the tube nucleus and a viable pollen grain is developed that is capable of successful fertilization. Microspores that preferentially go on to form microspore-derived embryos (MDEs) do not form a bi-nucleate stage or a tube cell nucleus nor are they able to fertilize the female reproductive structure of the plant. MDEs are produced directly from uni-nucleate microspores that are not permitted to develop into pollen. Therefore, Hawkes et al cannot support a 102 novelty or a103 obviousness rejection of the present claims. Withdrawal of this rejection is respectfully requested.

103(a) Rejection – Kmiec '181 in View of Fennell et al

Claims 24 and 28-32 have been rejected under 35 USC 103(a) for being obvious in view of Kmiec '181 in view of Fennell et al. This rejection is respectfully traversed.

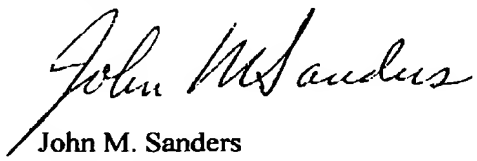
The Examiner has used Kmiec '181 for teaching the use of MDON to alter plant genes and Fennell et al for teaching the **TRANSFORMATION** of plant microspores. While Fennell et al does teach the introduction of DNA ("foreign genes") into

microspores, it **CANNOT** support a 103(a) rejection in combination with Kmiec '181 because Fennell et al only teaches the use of full length genes with regulatory regions that are inserted into the genome **randomly**. The MDON of the present invention are different from the "DNA expression cassettes" of Fennell et al both in (1) size and (2) chemical composition. The MDON is a relatively small molecule and results in a targeted mutation of at least one nucleotide in a predetermined site of the genome as opposed to the random insertion of a large transgene molecule. Fennell et al shed no light on the predictability of MDON and cannot support an obviousness rejection. Withdrawal of this rejection is respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Respectfully submitted,



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Attachment: Revocation of Power of Attorney and New Power of Attorney